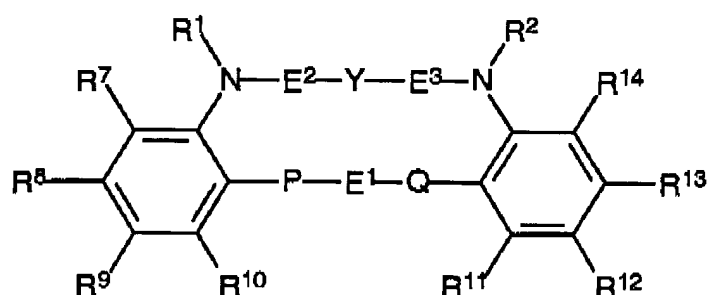


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REMARKS

The Claimed Invention

The present invention is directed to derivatives of crown ether compounds that are required to comprise a dye, a reactive group or a conjugated substance. These crown ether compounds have the following general structure:



wherein the substituents are as defined in the claims. The present crown ether compounds bind sodium, calcium and potassium ions under physiological conditions and when attached to a fluorophore are fluorogenic ion indicators. Thus, these crown ether compounds find particular use as indicators of said metal ions wherein they demonstrate a changed fluorescent signal when bound to ions such as sodium.

The Pending Claims

Prior to consideration of the following Response to Office Action, Claims 1, 3, 5-10, 12, 14-21, 25-32 and 34-55 are pending. Claims 1, 3, 5-10, 12, 14-20 and 52-54 are directed to the present crown ether compounds comprising at least one -L-DYE, -L-Rx or -L-Sc. Claims 21, 25-32, 34-43 and 55 are directed to the present crown ether compounds wherein the compounds comprise at least one -L-DYE. Claims 44-50 are directed to a method for detecting target metal ions in a sample using the present crown ether compounds. Claim 51 is directed to a kit for detecting or quantitating target metal ions.

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The Office Action

Claims 1, 3, 5-10, 12, 14-21, 25-32 and 34-55 are subject to a restriction requirement.

Amendments

Claims XX have been amended.

Applicants believe that no new matter has been added by any of these amendments and the Examiner is respectfully requested to enter them.

RESPONSE TO THE RESTRICTION REQUIREMENT

In the response that follows, the Examiner's Election/Restriction of the Applicant's claimed invention is provided in full text, as identified by indented small bold print, followed by the Applicants response.

Applicant's amendments and remarks filed 02/19/04 have been received and reviewed. Claims 1,3,5-10, 12, 14-21,25-32 and 34-55 are now pending in this application. After further review of the claims and Applicants remarks, it was deemed that a restriction requirement is necessary because the search and examination of the entire scope of the claims places an undue burden on the office. Each "core" and each "Sc" group supports a different patent.

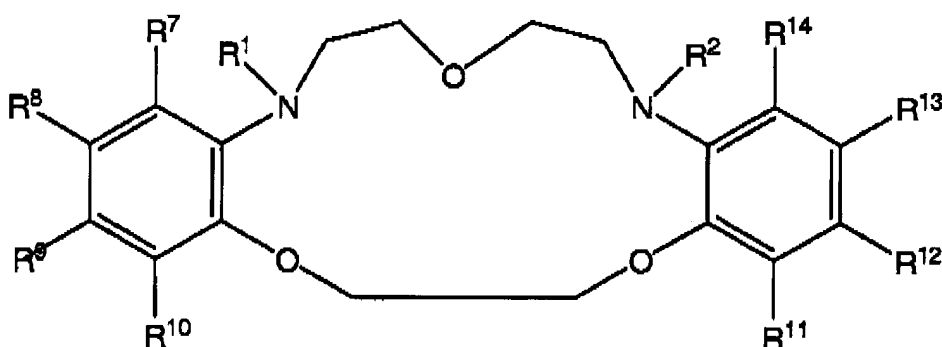
Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. **Claims 1,5-10, 12, 15-21,31,32,36-40,42,43 and 52-54, drawn to compounds and compositions of the compound of claim 1 wherein E1, E2 and E3 are ethylene groups and Y, P and Q are -O-, classified in class 540, subclasses 451, 452, 454, 455 and 469.**
- II. **Claims 1,3,5-10, 12, 14-21,25-32 and 34-55, drawn to compounds, compositions, methods of use and a kit which subject matter is not embraced by group I above. Should Applicants elect this group, further election of a specific "core" and "Sc" is required. Classifications of all of the compounds, the protein, polysaccharide, biotin, polymer, nucleoside, drug, cell, virus, etc. and method of detecting a target, and the kit is too burdensome.**

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Applicants respectfully traverse the above restriction requirement and request reconsideration, but as required by CFR 1.143 Applicants provisionally elect group I as drawn to compositions and compounds wherein E¹, E² and E³ are ethylene groups and Y, P and Q are -O-. These compounds having the following formula:

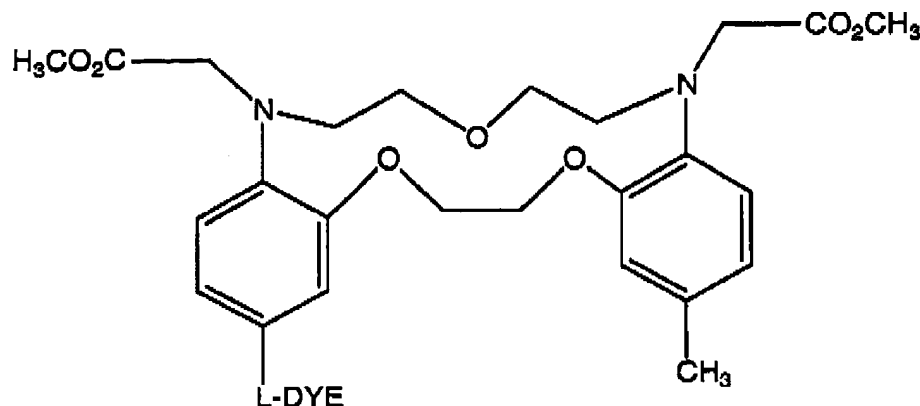


wherein at least one of R¹, R², R⁷, R⁸, R⁹, R¹⁰, R¹¹, R¹², R¹³ and R¹⁴ is -L-DYE, -L-So or -L-Rx (See, Claim 1).

Applicants traverse the restriction requirement and respectfully request that the Examiner reconsider re-joining the claims (Groups I and II). Applicants would first like to highlight the salient points of the prosecution to date as it bears on the present argument for re-joining the claims.

1. In a first office action (mail date 5/28/03) the Examiner issued an Election requirement without any comments about restricting the claims.
2. In the response to this office action (filed 6/16/03) Applicants elected 1,18-bis(methoxycarbonylmethyl)-14-methyl-5-[TMR]-DDTCPD for the purposes of initiating a search and examination of the present claims. The elected compound has the following structure:

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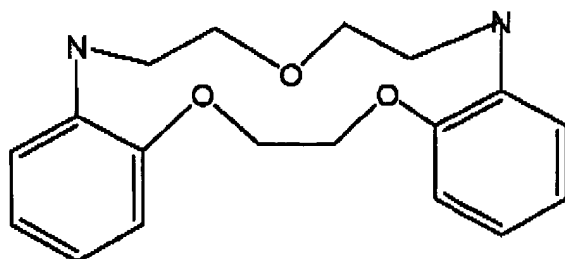


At that time Applicants requested, "when the elected species is found patentable that the Examiner expand the scope of the searching and examination to include the other presently claimed crown ether compound".

3. However, in the following office action from the Examiner (mail date 8/19/03) the Examiner withdrew claims 21-41 and 44-51 because the Applicants had not traversed the restriction requirement of the first office action. Applicants argued that there was no restriction requirement made by the Examiner and that the withdrawing the claims was improper. Applicants would herein like to note that the claims, which the Examiner improperly withdrew, were method and kit claims, wherein the Examiner stated, "Claims 21-41 and 44-51 are withdrawn from consideration because they are drawn to *methods and kits that raise different issues of patentability and require separate searches*" (emphasis added).

The Examiner did however state, "the elected compound was not found in the search and is allowable. The search was expanded to embrace the core

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Thus, compounds of this scope of the core identified above along with the definitions of the variable have been examined. The Examiner cited no art and issued no 102 or 103 rejections, thus indicating that this core structure and corresponding R groups are allowable.

Applicants respectfully assert that this core structure that was previously Examined and stated by the Examiner to be allowable is the same scope of the compounds in current group I. Thus, since the Examiner has previously stated this group to be allowable, Applicants respectfully request that the search and examination be expanded to cover other presently claimed compounds or at a minimum indicate that these claims are allowable.

4. The Applicants response to Office Action (filed 2/19/04) argued that withdrawing the claims was improper because there no was no restriction requirement as provided by in the MPEP. MPEP 803.1 states that when issuing a restriction requirement "Examiners must provide reasons and or reasons to support conclusions".

Based on the Examiner's previous remarks of record and the current office action (mail date 4/19/04), which the Applicants are hereby responding to, Applicants respectfully request that 1) the Examiner expands the scope of the compounds to be examined beyond those that he has already stated have been examined and found allowable, and 2) due to this that group I be re-joined with group to for an expanded scope. It would appear to be in everyone's best interest to expand the scope until an art reference is found that appears to be relevant to the patentability of the presently

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claimed rather than to put off the search when a divisional patent application is filed. Applicants would like to suggest initially expanding the scope wherein Y is S or NR⁴.

Furthermore, Applicants would like to draw the attention of the Examiner to the specific claims in the groups, which he has designated group I and II based on the core structure of the compound. Applicants have provisionally elected the compounds wherein E¹, E² and E³ are ethylene groups and Y, P and Q are -O-, which the Examiner has stated are in group I and encompass claims 1,5-10, 12, 15-21,31,32,36-40,42,43 and 52-54. The Examiner has further stated that all other compounds and subject matter are grouped into group II, claims 1,3,5-10, 12, 14-21,25-32 and 34-55. Applications respectfully assert that based on the compound stated by the Examiner that this grouping is incorrect. Thus, if the Examiner chooses not to re-join the claims of group I and group II, the Applicants request that the claims be appropriately grouped based on the compound elected.

Such a grouping that embraced the elected compound would include Claims 1 (in part), 5, 6, 7, 8-9 (in part), 10, 12, 14, 15, 16-21 (in part), 25-30, 31-32 (in part), 34-35, 36-41 (in part), 42-43, 44-47 (in part), 48-49, 50 (in part), 51, 52 (in part), 53, 54, 55 (in part). A group including other compounds and subject matter would include the Claims 1 (in part), 3, 8-9 (in part), 16-21 (in part), 31-32 (in part), 36-41 (in part), 44-47 (in part), 50 (in part) and 52 (in part). Applicants respectfully request that the claims be appropriately grouped based on the Examiner's argument to ensure that what he has designated as independent inventions are in one group of claims and not spread across groups.

**The inventions are distinct, each from the other because of the following reasons:
The claims are not drawn to art recognized equivalents. Groups I and II are drawn to structurally dissimilar compounds. They are made and used independently. They are independent and patentably distinct.**

Applicants respectfully assert that the inventions of group I and II are not distinct or independent because the compounds are not made or used independently. All the compounds, compositions and methods of the present invention are used to detect a target metal ion in a sample wherein the choice of core substituents tune the affinity and specificity of the metal ion.

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The Examiner has stated that the present application contains both independent and distinct inventions. MPEP 806.04 states that "two different combinations, not disclosed as capable of use together, having different modes of operation, having different functions or different effects are independent". As indicated by the Examiner, MPEP 806.04 indicates that for inventions to be independent they must satisfy the following criteria; they are not disclosed to be used together and one of the following, different modes of operation, different functions or different effects. Therefore to be properly considered independent the inventions need to fulfill the first requirement and at least one of the next three. All of the claimed compounds are disclosed to be used together, with the same mode of operation, effect and function. Thus, the Applicants respectfully assert that the presently claimed inventions are not independent. In addition, the inventions are not distinct as defined in the MPEP 806.05(c). Applicants respectfully request that the Examiner reconsider the restriction requirement and request that the claims be re-joined.

If, say compounds of Group I, were anticipated, applicants would not acquiesce in the rejection of Group II thereover or vice-versa. They are patentably distinct. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, and because the search required for Group I is not required for Groups II, restriction for examination purposes as indicated is proper.

Note that compounds, corresponding compositions, a method of use and a process of making that are of the same scope are considered to form a single inventive concept. The instant claims are not so linked as to form a single inventive concept. The compounds are so diverse in scope that a prior art anticipating one compound under 35 USC 102 would not render obvious another compound of the same claim under 35 USC 103.

Applicants appreciate that the Examiner has stated on the record that "compounds, corresponding compositions, a method of use and a process of making that are of the same scope are considered to form a single inventive concept". However, in an earlier office action (mail date 8/19/03) the Examiner stated (also on the record), when prematurely withdrawing the method and kit claims, "...methods and kits raise different issues of patentability and require separate searches". Thus, the restriction requirement would appear to be subjective based on the Examiner and not a set of requirements set out in the MPEP. In one instance the Examiner has stated that the present application includes distinct inventions because the application includes claims

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directed at compounds, methods and kits. In a second instance the Examiner has stated, with no comment based on the earlier statement, that the present application contains distinct inventions based on the scope of the compounds – “The claims are not drawn to art recognized equivalents. Groups I and II are drawn to structurally dissimilar compounds”. As there seems to be some confusion on what forms a distinct invention, Applicants would simply request that the Examiner re-join groups I and II and expand the search and examination.

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CONCLUSION

In view of the above remarks and previous amendments, it is submitted that this application is now ready for allowance. Early notice to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned at (541) 335-0203.

Respectfully submitted,

Date: July 14, 2004

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